

**Abstract**

A method of preparing lipid particles having an asymmetric lipid coating is described. The lipid composition of the outer lipid coating of the particles varies from the inner to outer surfaces. The asymmetric lipid particles are formed by preparing a lipid composition containing a charged lipid and a therapeutic agent, where the particles each have an outer lipid coating with an external lipid leaflet and an internal lipid structure. The particles are then incubated under conditions effective to remove the charged lipid from the external lipid leaflet, thus rendering the lipid coating asymmetric. The particles have the ability to their regain surface charge via translocation of the lipids.